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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/581,269	06/01/2006	Stefan Arnold	LNK-009	3141

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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,269	ARNOLD ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 01 June 2006 has been entered in full. Claims 1-13 are pending and under examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statement(s)(IDS), filed 01 June 2006, was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 7 and 8 are rejected under 35 U.S.C. 102(e) as being anticipated by Canning et al., U.S. Patent No. 6,979,442 B1.

The instant claims are drawn to a stable pharmaceutical formulation of erythropoietin (EPO) containing tris-(hydroxymethyl)-aminomethane as a stabilizer, whereby the formulation does not contain amino acids or human serum albumin, wherein the formulation is an aqueous formulation, wherein the formulation pH ranges from 5.9 to 6.8, wherein tris-(hydroxymethyl)-aminomethane is present in an amount of 20 to 100 mM.

Canning et al. teach stabilized protein pharmaceutical compositions comprising stabilizing buffers (abstract). Canning et al. teach a composition comprising granulocyte-colony stimulating factor (G-CSF), wherein the stabilizing buffer is present in a concentration ranging from about 0.005M to about 2M (column 4, lines 28-31). Canning et al. teach other proteins suitable for the stabilized protein composition of the invention including erythropoietin (EPO) (column 9, lines 32-41 and column 10, line 27). Canning et al. teach "stabilizing buffer" to mean any of several buffers that when combined with the protein of the stabilized composition, provide for a stabilized protein composition. Canning et al. teach tris-(hydroxymethyl)-aminomethane as a stabilizing buffer (column 13, line 56-57). Canning et al. teach that the pH of the stabilized protein composition of the present invention can be in the range of from about 4.0 to about 8.0 (column 13, line 46-column 14, line 45).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canning et al. as applied to claim 1 above, and further in view of Sharma et al., U.S. Patent Application US 2003/0148938 A1 (reference submitted by Applicant) and Naeff et al, U.S. Patent No. 6,645,522 B2.

The teachings of Canning et al. are described above. Canning et al. do not teach a pharmaceutical formulation comprising EPO, tris-(hydroxymethyl)-aminomethane **and** sodium phosphate buffer and NaCl. Sharma et al. teach aqueous pharmaceutical compositions comprising EPO and a carboxymethyl ether cellulose polymer (para 0011-0023). Sharma et al. teach the use of sodium phosphate as a buffering agent in the pharmaceutical composition. Sharma et al. teach that the concentration of buffering ions will generally range from about 10 mM to about 30 mM (para 0037). Sharma et al. teach the use of NaCl as an ionic tonicity agent in the pharmaceutical composition. The use of

NaCl as a tonicity agent is employed at a concentration of about 75 mM to about 100 mM (para 0039). Naef et al. teach an EPO liposomal-based dispersion composition comprising sodium phosphate buffering agents sodium dihydrogen phosphate dehydrate and disodium hydrogen phosphate dehydrate (column 2, lines 22-45; column 4, lines 21-29 and claims).

All of the elements parts in the instant composition are disclosed in Canning, Sharma and Naef. The only difference is the combination of the "old elements" into a single composition. In combination, each element (in the instant case sodium phosphate and NaCl) would have performed the same function as it did separately. Thus, it would have been obvious to one having ordinary skill in the art to combine EPO and tris-(hydroxymethyl)-aminomethane with sodium phosphate buffer and NaCl because Sharma and Naef teach the use of sodium phosphate to achieve the predictable results of buffering compositions comprising EPO to the desired pH. Shaef et al. also teach the use of NaCl in compositions comprising EPO to achieve the predictable results of rendering EPO formulations iso-osmotic.

Claims 9-11 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Canning et al. as applied to claim 1 above, and further in view of Woog et al., U.S. Patent No. 4,992,419 (reference submitted by Applicant).

The teachings of Canning et al. are described above. Canning et al. do not teach a pharmaceutical formulation comprising EPO, tris-(hydroxymethyl)-aminomethane **and** a non-ionic detergent. Woog et al. teach pharmaceutical compositions comprising EPO

(abstract and column 2, lines 20-40). Woog et al. teach that adhesion of EPO on the ampoule walls and syringes is reduced by the addition of small amounts of detergent. Concentrations of detergents from 0.05 to 5 g./liter and especially of from 0.1 to 0.5 g./liter have proved to be useful. Woog et al. teach non-ionic wetting agents, such as the various polymacrogol types, Tween 20, Tween 80 and sorbitan trioleate (column 3, lines 1-10).

All of the elements parts in the instant composition are disclosed in Canning and Woog. The only difference is the combination of the "old elements" into a single composition. In combination, each element (in the instant case a non-ionic detergent) would have performed the same function as it did separately. Thus, it would have been obvious to one having ordinary skill in the art to combine EPO and tris-(hydroxymethyl)-aminomethane with a non-ionic detergent such as Tween 20 or Tween 80 because Woog et al. teach the use of non-ionic detergents in compositions comprising EPO to achieve the predictable results of reducing adhesion of EPO on the ampoule walls and syringes.

Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Canning et al. as applied to claim 1 above, and further in view of Konings et al., U.S. Patent No. 5,376,632. The teachings of Canning et al. are described above. Canning et al. do not teach a pharmaceutical formulation comprising EPO, tris-(hydroxymethyl)-aminomethane **and** ethylenediaminetetraacetic acid in an amount of 0.1 to 0.5 mM. Konings et al. teach methods for stabilizing pharmaceutical compositions comprising

EPO in an aqueous solution (abstract; column 4, lines 41-60). Konings et al. teach that trace amounts of heavy metal ions catalyze the degradation of EPO, thus it may further be appropriate to add a suitable complexing agent such as calcium chloride or ethylenediaminetetraacetic acid (i.e. EDTA). Konings et al. teach that for example calcium chloride may be added at a concentration of 0.02-2 g/l (i.e. 0.1 to 0.5 mM).

All of the elements parts in the instant composition are disclosed in Canning and Konings. The only difference is the combination of the "old elements" into a single composition. In combination, each element (in this case ethylenediaminetetraacetic acid) would have performed the same function as it did separately. Thus, it would have been obvious to one having ordinary skill in the art to combine EPO and tris-(hydroxymethyl)-aminomethane with EDTA because Konings et al. teach the use of EDTA in compositions comprising EPO to achieve the predictable results of reducing the degradation of EPO.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (571) 272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

RMD
8/15/07

/Gary B. Nickol/
Supervisory Patent Examiner, Art Unit 1646